Caveat Oncologist: Clinical Findings and Consequences of Distributing Counterfeit Erythropoietin in the United States

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Abstract

Purpose: Counterfeit pharmaceuticals pose risks domestically. Because of their cost, cancer pharmaceuticals are vulnerable. We review findings from a domestic counterfeiting episode involving erythropoietin and outline anticounterfeiting recommendations for policy makers, patients, and health care professionals.

Materials and Methods: Information was obtained on patients who received counterfeit erythropoietin, its distribution, and criminal investigations into counterfeiting networks. Interview sources included a physician, an attorney, employees of the Florida Department of Health and Human Services and the US Food and Drug Administration's (FDA) Office of Criminal Investigation, manufacturers, and wholesalers. Other sources included the book "Dangerous Doses," LexisNexis (search terms "counterfeit" and "erythropoietin") and the FDA database.

Results: Counterfeit product consisted of 2,000 U vials with counterfeit labels denoting 40,000 U. The counterfeiters, in collaboration with a Miami pharmacy, purchased 110,000 erythropoietin 2,000 U vials and affixed counterfeit labels to each vial. Products were then sold via the pharmaceutical "gray market" to wholesalers, then pharmacy chains. Investigations by Florida government officials implicated 17 persons, all of whom were found guilty of trafficking in counterfeit pharmaceuticals. Despite the large size of the operation, the FDA received reports of only 12 patients who had received counterfeit erythropoietin and detailed information for only two individuals. A 17-year-old liver transplant recipient and a 61-year-old patient with breast cancer experienced loss of efficacy after receiving counterfeit erythropoietin.

Conclusion: Wider use of FDA anticounterfeit initiatives, limiting pharmaceutical suppliers to reputable distributors, and educating providers and patients about signs of counterfeit drugs can improve the safety of cancer pharmaceuticals.

Introduction

Counterfeit pharmaceuticals are an increasingly important safety concern. Counterfeit drugs are defined under federal law as those sold under a product name without proper authorization.[1] They include pharmaceutical packages that differ from what is stated on the affixed label, including having smaller amounts of active ingredient, wrong ingredients, or no active ingredients (designated "fake fakes"). Counterfeit pharmaceuticals may contain stated amounts of active ingredients but not be made by the indicated manufacturers, or the vials may have counterfeit labels or fake expiration dates (designated "real fakes").[2,3]

Although lay press articles primarily link counterfeit drugs to Internet sales and foreign countries, pharmaceuticals purchased at local pharmacies or national pharmacy chains may also be counterfeit. The US Food and Drug Administration (FDA) reports an 800% increase in the number of new counterfeit cases between 2000 and 2006.[3] The ideal target for counterfeiting is high-cost, parentally administered medications packaged in vials.[4] Consequently, medications for the treatment of cancer and HIV head the list. One of the largest drug safety breaches involved purchase of counterfeit erythropoietin products by an estimated tens of thousands of patients, many of whom had been diagnosed with cancer.[5]

Herein, we report case histories of persons who received counterfeit erythropoietin products; review subsequent federal, state, and private sector initiatives designed to protect against counterfeit pharmaceuticals; and outline efforts that patients, health care professionals, and policy makers can take to protect the cancer community against counterfeit pharmaceuticals. To our knowledge, no previous article has reported clinical findings associated with the use of any counterfeit pharmaceutical product, the extent of the breaches in the security of the pharmaceutical distribution chain implicated in the domestic distribution of counterfeit erythropoietin, or the extent to which underreporting of counterfeit erythropoietin cases occurred.

Domestic counterfeiting is facilitated by complex pharmaceutical distribution systems, wherein pharmaceutical products are extensively intermingled.[3,6] After leaving manufacturers' loading docks, pharmaceuticals move through a maze of middlemen who buy, sell, and repackage them. Three national distributors—Cardinal, AmerisourceBergen, and McKesson—control 90% of pharmaceutical distribution and generate annual revenues of $150 billion. Secondary and tertiary distribution levels consist of 15 major regional wholesalers and many small, poorly regulated regional wholesalers (termed the "gray market").[7] The gray market serves small hospitals, pharmacies, and medical practices. Once introduced into the distribution chain, counterfeit pharmaceuticals can become mixed with real pharmaceuticals and subsequently be distributed to large numbers of unsuspecting providers and patients. Clinically, coun-

terfeit pharmaceuticals are difficult to differentiate from real products.

The Federal Prescription Drug Marketing Act (PDMA), signed into law in 1988 and amended in 1992, is the primary law ensuring pharmaceutical distribution safety.[8] Section 503(e)(1)(A) requires that ". . . each person who is engaged in the wholesale distribution of a drug who is not the manufacturer or authorized distributor of record of such drug provide to the person who receives the drug a statement (in such form and containing such information as the Secretary may require) identifying each prior sale, purchase, or trade of such drug (including the date of the transaction and the names and addresses of all parties to the transaction)." Amendments (21 CFR Part 203) require that wholesalers be provided a drug "pedigree" (a statement of origin that identifies each prior sale, purchase, or trade of a drug, including the date of those transactions, and requires that the names and addresses of all parties to them be retraceable to the first sale by the manufacturer).[9] Implementation of the pedigree requirements is problematic, and most states are unable to conduct regular inspections of wholesalers to ensure compliance with the law. The Food, Drug, and Cosmetic Act (21 U. S. C. §301), signed into law in 1939, requires that drugs be appropriately labeled.[10] Federal trademark law has also been recruited to fight counterfeit pharmaceuticals, imposing a penalty of 10 years imprisonment for violation of the PDMA.[11] Initially, implementation of regulations against counterfeit pharmaceuticals was deferred by the FDA in anticipation that distributors would voluntarily adopt electronic "track and trace" technology such as radiofrequency identification devices (RFIDs). When this technology failed to emerge, the FDA implemented a scaled-down pedigree requirement in 2006.[12] Trademark law was subsequently amended to broaden the definition of trafficking and eliminate a loophole in the law (previously, trafficking in trademarks not attached to a product did not violate the relevant statutes) to ensure imposition of penalties for transfers of counterfeit goods.[13]

Materials and Methods

Information was obtained from interviews with a physician and an attorney for one of two affected patients, officials of the Florida Department of Health and Human Services, the FDA's Office of Criminal Investigation, counterfeit protection divisions of pharmaceutical manufacturers, and wholesale suppliers of pharmaceuticals. Print sources included the book "Dangerous Doses" (an investigative journalism report on counterfeit pharmaceutical episodes in the United States).[5] Electronic sources for the years 2002 to 2010 included materials identified in PubMed, LexisNexis, and Google searches (key search terms "counterfeit pharmaceuticals" and "erythropoietin"), and materials disseminated by the FDA, Healthcare Distribution Management Association, the FDA's Counterfeit Alert Network, and the Pharmaceutical Security Institute. Search terms for the FDA's MedWatch database analysis included "medication tampering" and "pharmaceutical product counterfeit" for the years 1998 to 2010. Additional analysis of FDA databases was performed using Medloom proprietary technology, which evaluates associations between adverse events and individual drugs in the FDA MedWatch database by using artificial intelligence–based statistical early signal detection algorithms.[14]

Results

FDA Reports and Analysis

Between 1998 and 2010, the FDA's Adverse Event Reporting System (AERS) received reports of 12 cases of persons who had received erythropoietin that included the term "medication tampering, " accounting for the third largest number of reports of medication tampering in the database. Propofol (n = 113) and heparin (n = 84) were the first and second most common injectable drugs listed under this term. The only AERS reports of "pharmaceutical product counterfeit" for injectable drugs were for heparin (n = 3) and fentanyl (n = 7). A statistical analysis of the 50 most significant drug/adverse event associations included in the FDA's AERS database revealed significant associations between "erythropoetin" and "drug ineffective" for the fourth quarter of 2002 and the first and second quarter of 2003, and in no other reporting periods. Of note, similar associations were not discerned for any other injectable pharmaceutical agent.

Case Histories

Detailed case histories and information on sources of the counterfeit product were available for two patients.[5] The first, a 17-year-old liver transplant recipient, was treated in 2002 with erythropoietin in vials purportedly containing 40,000 U. The vials were purchased at a Manhattan CVS pharmacy and actually contained 2,000 U of erythropoietin (Appendix Figure A1, online only). Counterfeit labels had been affixed to the vials (termed "up-labeled" counterfeits) in the backyard of a strip club in Miami. The patient was administered up-labeled erythropoietin vials for 8 weeks and developed anemia (hemoglobin levels decreased from 12 mg/dL to 8 mg/dL) over this period. A few hours after each injection of up-labeled vials, the patient experienced severe muscle cramps near the injection site. The counterfeit product was detected when the patient's nurse read a "Dear Healthcare Professional" letter[15] from the manufacturer indicating that up-labeled erythropoietin vials had been confiscated from pharmaceutical distributors in several states. Although the lot number on the up-labeled vials did not match any of the lot numbers included in the letter, the nurse identified a typographical misprint in the counterfeit label (absence of a degree symbol next to the storage directions).

The second patient, a 61-year-old woman with recurrent breast cancer, was treated with up-labeled erythropoietin for 8 weeks in 2002.[5] Treatment with the counterfeit product was complicated by loss of efficacy (hemoglobin levels reportedly decreasing from normal to anemic levels), but there were no injection site reactions. The patient's nurse read a Dear Healthcare Professional letter from the manufacturer describing up-labeled vials of erythropoietin confiscated from regional distributors in several states.[15] The nurse noted that the lot number on the patient's erythropoietin vial was the same as the lot

number reported in this letter and that typing imperfections on the vial matched those described in the letter. Shortly thereafter, the patient's breast cancer became more aggressive and she died as a result of the disease.

Criminal Investigations

Two agents with the Bureau of Statewide Pharmaceutical Services of the Florida Department of Health initiated the investigation of counterfeit erythropoietin in 2002.[5] Subsequently, a state prosecutor formed an investigative task force. A task force member was informed by a small pharmacy owner in Miami that a wholesaler wanted to sell erythropoietin 40,000 U/mL vials at markedly discounted prices. The task force member posed as a buyer and confiscated these vials. The "pedigree" attached to the shipping manifest indicated that the manufacturer had sold the product to a Houston wholesaler, who in turn had sold the product to a Dallas wholesaler. However, records from the manufacturer indicated that no erythropoietin had been sold to either wholesaler. The order for erythropoietin at the Miami pharmacy was large enough to supply the anemia treatment needs of patients with cancer and patients undergoing dialysis in the entire states of Florida and Georgia. Testing of the contents of the up-labeled vials by the manufacturer indicated that each vial contained 2,000 U/mL of erythropoietin, although counterfeit labels stated that the vials purportedly contained 40,000 U/mL. The pharmaceutical manufacturers issued Dear Health Care Professional letters describing the counterfeit operation, lot numbers on the vials of counterfeit erythropoietin, and printing discrepancies on the counterfeit labels that distinguished them from labels affixed to unadulterated pharmaceuticals.[15] In response, officials at the manufacturers and the FDA received numerous calls from pharmacies, hospitals, and patients who had purchased up-labeled vials. These calls identified an Illinois hospital that had received 1,617 vials of counterfeit erythropoietin from an AmerisourceBergen warehouse in Kentucky, which in turn had purchased up-labeled vials from wholesalers in Tennessee and Georgia. Another investigation identified a medical supply warehouse in Texas with 1,004 vials of erythropoietin that lacked authenticating pedigree documents.[5]

Criminal investigations facilitated reconstruction of the route by which counterfeit erythropoietin had traveled in 2002 (Figure 1). The product's manufacturer sold 2,000 U/mL vials of erythropoietin to national distributors, who then sold 27,000 boxes of these vials to the Miami pharmacy. The pharmacy sold these vials to a middleman who partnered with a counterfeiter. The counterfeiter affixed 40,000 U/mL labels to vials that contained 2,000 U/mL of erythropoietin. These vials were sold to small regional wholesalers, who in turn unwittingly sold the counterfeit product to discount purchasing programs of AmerisourceBergen, which then sold up-labeled product to CVS Pharmacy. A Manhattan branch of CVS Pharmacy dispensed two packages of counterfeit erythropoietin vials to the liver transplant recipient. AmeriSourceBergen also sold up-labeled vials to wholesalers in Texas, Florida, Tennessee, and New York, who then sold these vials to a regional wholesaler in Arizona. A local Missouri pharmacy purchased several counterfeit vials from the Arizona wholesaler, who then sold the product to the patient with breast cancer.

Although Federal investigators confiscated 13,000 up-labeled vials of erythropoietin from regional wholesalers in Texas, Michigan, Illinois, and Florida, 97,000 counterfeit vials were not recovered. Task force investigations resulted in 64 subpoenas, 12 search warrants, confiscation of $14 million in counterfeit medicines, and a return of $3 million in assets to Florida Medicaid. The task force investigated other counterfeit instances, including one that resulted in seizures and recalls of counterfeit atorvastatin. In 2003, a Florida grand jury indicted 17 coconspirators for allegedly trafficking in counterfeit pharmaceuticals. The middlemen were charged with racketeering, unauthorized scheme to defraud, unauthorized sales of prescription drugs, and relabeling vials of erythropoietin. In 2003, 16 individuals pled guilty to criminal charges. In 2008, the leader of the counterfeit ring received a 12-year prison sentence for distributing counterfeit pharmaceuticals (he had been in prison since 2003). Subsequently, informants notified the manufacturer that another individual in Miami was distributing vials of counterfeit erythropoietin. The manufacturers again issued Dear Healthcare Professional letters.[16] FDA agents bought suspected counterfeit vials from this individual at a shopping mall, and FDA laboratories discovered that these vials contained bacterially contaminated water. Three individuals pled guilty to criminal charges of distributing counterfeit pharmaceuticals.[5]

Discussion

One to three percent of pharmaceuticals sold by major distributors are purchased from regional secondary wholesalers who constitute the majority of the gray market distribution chain, an at-risk link in the pharmaceutical supply chain.[7]A poorly regulated gray market can allow counterfeit products to mix with noncounterfeit products. Federal legislation related to anticounterfeiting measures targeting the gray market has been delayed for at least a decade, primarily as a result of lobbying by pharmaceutical and retail industries. Filling this void, anticounterfeiting initiatives have been undertaken by federal policy makers, the FDA, state legislatures, investigative branches of state governments, pharmaceutical manufacturers and distributors, and pharmacy chains (Figure 2).

The FDA initiated large-scale anticounterfeiting efforts in 2003, when it established a Counterfeit Drug Task Force.[17] The first Counterfeit Drug Task Force Report supported a multipronged strategy to secure the drug supply, including requiring manufacturers to use anticounterfeit packaging technologies.[17] The 2004 Report urged enacting legislation increasing criminal penalties against persons convicted of trafficking in the manufacture or distribution of counterfeit pharmaceuticals and recommended funding for international anticounterfeiting investigations.[18] In the 2005 report, the use of RFID tags and e-pedigrees for products was emphasized.[19] In the 2006 report, policy

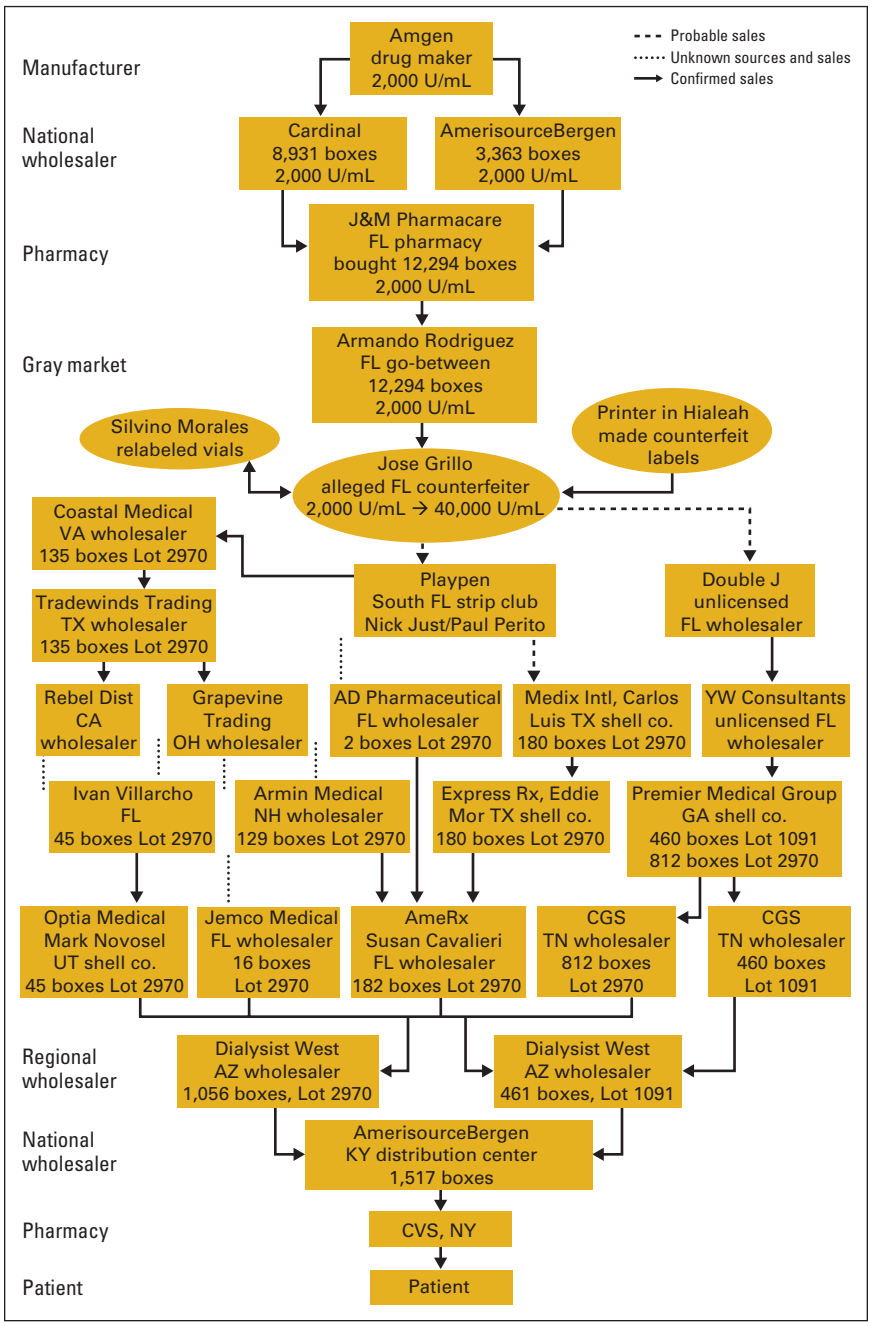

Figure 1. Reconstruction of the route traversed by counterfeit erythropoietin. Adapted from Eban K: Dangerous Doses: How Counterfeiters Are Contaminating America's Drug Supply. New York, NY, Harcourt, 2005. Used with permission.

makers recommended that distributors maintain pharmaceutical "pedigrees."[20] No additional reports have been disseminated since 2006.

The FDA established a Counterfeit Alert Network that provides alert messages about counterfeit drug incidents; describes measures to take to minimize exposure (eg, recall information); and outlines roles that consumers, health professionals, and wholesalers can play in protecting against counterfeit pharmaceuticals.[21] It consists of a network of national organizations, consumer groups, and industry representatives. Of note, no oncology-focused organization has joined the Network.

The FDA's AERS database was not a highly useful source of information on counterfeit erythropoietin. The absence of cases of erythropoietin associated with "pharmaceutical product counterfeit" in AERS was disappointing because in 2002 and 2003, the FDA and manufacturers extensively publicized the incident as one associated with distribution of large numbers of counterfeit erythropoietin vials. When a product has altered labeling or is identified as contaminated or subpotent, reporters of adverse drug reactions to the FDA should include the term "pharmaceutical product suspected counterfeit," so that these problems can be identified more rapidly. It was more reassuring

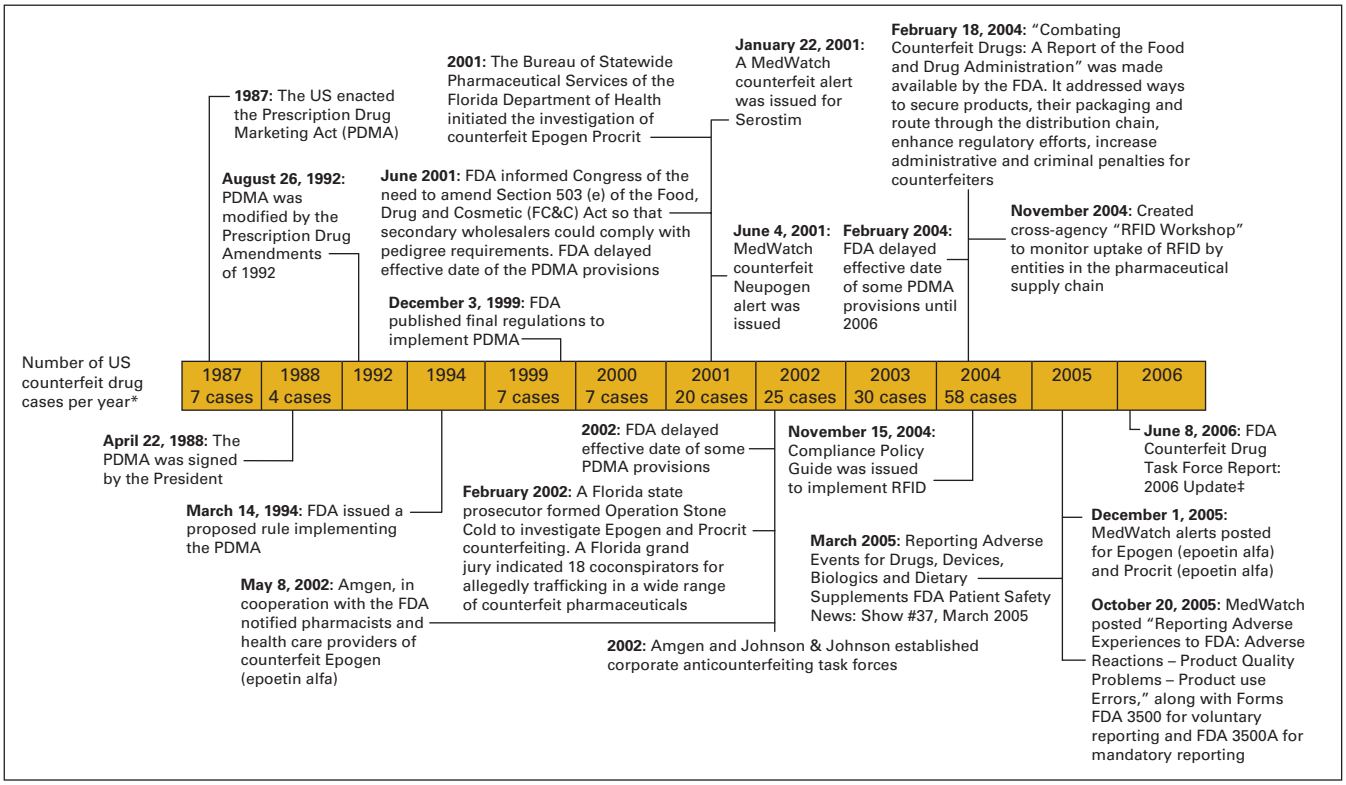

Figure 2. Timeline of federal response to counterfeit drugs. Although the US government has been implementing policy changes designed to curb counterfeit drug activity, the actual number of counterfeit drug cases per year reported to the FDA increased 800-fold between 2000 and 2006. FDA, US Food and Drug Administration; RFID, radio frequency identification.

that artificial intelligence–based statistical analyses of the FDA AERS database highlighted safety concerns with erythropoietin during 2002 and 2003, by analyzing reports of drugs associated with "loss of efficacy."[14]

State-level anticounterfeit initiatives require "pedigree" requirements for certain prescription drug transactions, strengthen felony charges for trafficking in counterfeit pharmaceuticals that result in death, allow officials to conduct background checks of wholesale distributors, and increase regulation over pharmaceutical wholesalers and distributors.[22]

Pharmaceutical manufacturers established corporate anticounterfeiting taskforces, added counterfeiting information to their Web sites, regularly consulted with the FDA on counterfeit issues, and issued warning letters outlining suspect lot numbers during at-risk periods. Some manufacturers discontinued selling pharmaceuticals to wholesalers who purchased products from gray market sources. Several manufacturers made physical packaging changes, adding tamper-resistant seals and holograms. However, these measures might prove ineffective, as licensed repackagers often break seals when distributing smaller allotments to drug stores and other outlets.

Private sector anticounterfeiting initiatives have occurred over the past decade. The Healthcare Distribution Management Association (HDMA), the National Association of Chain Drug Stores, the National Association of Boards of Pharmacies, and manufacturers and anticounterfeiting security organizations have strengthened their anticounterfeiting positions. While integrity in packaging is stressed, these groups have also resisted national all-inclusive pedigree requirements, believing that such requirements would adversely affect prices and decrease efficiency. The HDMA has taken on three different initiatives: in-transit cargo security measures, suspicious order monitoring, and advocating uniform pedigree standards at the state-level (realizing that uniform pedigrees are not likely to be accepted nationally). Another private sector activity, Verified-Accredited Wholesale Distributors accreditation, identifies legitimate and legally operating wholesale distributors and verifies compliance with state and federal laws for wholesale distribution. However, obtaining this accreditation is voluntary. Primarily because of product safety and diversion concerns, Cardinal Health closed its secondary trading division.[23] CVS also discontinued purchasing drugs from gray market distributors. Many pharmaceutical wholesale distributors have adopted practices wherein they purchase cancer pharmaceuticals directly from the manufacturer and ship directly to health care providers, eliminating involvement with the gray market.

Cancer-specific anticounterfeiting initiatives are emerging. The large cancer organization, US Oncology, instituted an ePedigree system that follows cancer drugs from the manufacturer to the patient. The system tracks the path of each drug through the supply chain; verifies that information in the pedigree has not been altered; and provides automatic self-authentication through encryption, using industry-standard technologies. Nationally, cancer pharmacists are advised to establish business practices that protect product integrity, closely inspect product at the time of delivery and at the time of dis-

pensing, and educate patients about signs of possible counterfeit pharmaceuticals (bad taste or odor, loss of efficacy, or unexpected injection site reaction, for example). Pharmacies are encouraged to purchase products from reputable sources and to notify staff and patients when products are purchased from different manufacturers, particularly for generics. Undoubtedly, the presence of a multitude of different marketing channels for each pharmaceutical agent makes this a Herculean task.

For patients with cancer, instances of loss of efficacy or injection site reactions or infections should raise concern that counterfeit drugs may have been administered. Most counterfeit safety signals are identified by patients. Therefore, physicians, nurses, and pharmacists play a key role in reporting patient concerns over possible counterfeit drugs to the FDA's MedWatch program.

A limitation of this review is the underreporting of information on counterfeit pharmaceuticals in the medical literature. Although an estimated 110,000 persons received counterfeit erythropoietin, the FDA's AERS program received information on only 10 of these cases and detailed clinical information for only two. In contrast, the recent episode of tampered heparin imported from China has been described in detail in the medical literature.[24] Underreporting of case histories to the FDA's MedWatch program was less of a concern with the heparin cases, presumably because of the high percentage of patients who developed clinical symptoms or died after administration of contaminated heparin. The FDA's MedWatch program received reports of 238 deaths associated with contaminated heparin. Underreporting of counterfeit pharmaceuticals in general is an international safety problem. Between 2002 and 2004, the World Health Organization received no reports of counterfeit pharmaceuticals.[25] A PubMed search fails to identify any other empiric clinical reports for any other counterfeit pharmaceutical, exclusive of the heparin incident. Finally, a distinction is made between counterfeit pharmaceuticals and biosimilars: generic biologic agents that, as a result of legislation in the Affordable Care Act, will be marketed in the United States in the near future. Biosimilars have already received regulatory approval in Europe and are extensively marketed there. To date, safety concerns with these agents have not been widely identified.

In 2004, Rudolph and Bernstein of the FDA's Office of Criminal Investigation wrote "that it will take some time for the United States drug supply to be secured effectively."[3(p1386)] Seven years later, it is clear that this has not occurred. Domestic pharmaceutical safety concerns, particularly for patients with cancer, are real, and a high level of vigilance is needed. Treating cancer with real pharmaceuticals is difficult enough. Treating this illness with counterfeit agents is impossible.

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References

1. US Food and Drug Administration: Counterfeit Medicine. http://www.fda.gov/oc/initiatives/counterfeit/qa.html

2. Federal Food, Drug and Cosmetic Act. U.S.C. §201(g)(2), 2004

3. Rudolf PM, Bernstein IB: Counterfeit drugs. N Engl J Med 350:1384-1386, 2004

4. National Association of Boards of Pharmacy: National Specified List of Susceptible Products. http://www.state.nj.us/health/eoh/slsdp.pdf

5. Eban K: Dangerous Doses: How Counterfeiters Are Contaminating America's Drug Supply. New York, NY, Harcourt, 2005

6. deKieffer D: Potential liability for counterfeit medications. J Pharm Pract 19: 215-220, 2006

7. ASHP congressional testimony on the "gray market" in pharmaceuticals. Am J Hosp Pharm 43:426-429, 1986

8. Prescription Drug Marketing Act of 1987, Public Law No. 100-293, 102 Stat. 95, 1987

9. Amendments of Prescription Drug Marketing Act of 21 CFR §§203.3, (u) and 203.50, 2006

10. Food and Drug Cosmetic Act of Pubic Law No 52 Stat. 1040:75-717, 1938

11. Lanham Trademark Act of U.S.C. §1051-1128, 1946

12. Draft Compliance Guide. Prescription Drug Marketing Act- Pedigree Requirements under 21 CFR Part 203. June 16, 2006. http://www.fda.gov/oc/initiatives/counterfeit/cpg.html

13. Trademark Dilution Review Act of Public Law 109-312, 2006

14. Better Living Through Technology. TMIS Newsletter. Orting, WV, TM Information Systems. http://www.tmis.org/enewsletters/2010-7-20.html

15. US Food and Drug Administration: MedWatch Safety Alerts for Human Medical Products. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/default.htm

16. US Food and Drug Administration: Procrit (epoetin alfa) Dear Healthcare Professional Letter Mar 2003. http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm167374.htm

17. US Food and Drug Administration: Counterfeit Drug Task Force Report October 2003 – THE COUNTERFEIT DRUG TASK FORCE. http://www.fda.gov/Drugs/DrugSafety/ucm174399.htm

18. US Food and Drug Administration: Counterfeit Drug Taskforce: Counterfeit Drug Task Force Report: February 2004 COMBATING COUNTERFEIT DRUGS. http://www.fda.gov/Drugs/DrugSafety/ucm173231.htm

19. US Food and Drug Administration: Counterfeit Drug Task Force Report: May 2005. Combating Counterfeit Drugs: A Report of the Food and Drug Administration Annual Update. http://www.fda.gov/Drugs/DrugSafety/ucm172935.htm

20. US Food and Drug Administration: Counterfeit Drug Task Force Report: June 2006. http://www.fda.gov/Drugs/DrugSafety/ucm172759.htm

21. US Food and Drug Administration: Counterfeit Alert Network. http://www.fda.gov/Drugs/DrugSafety/ucm170315.htm

22. Ling L: While we are waiting: Imagining and creating a safe drug supply while we await the coming of the radio frequency identification track-and-trace system. J Pharm Pract 19:153-160, 2006

23. Cardinal Latest Wholesaler to Curb Secondary Dealing. http://www.findarticles.com/p/articles/mi_m3374/is_7_27/ai_n13788235

24. Blossom D, Kallen A, Patel P, et al: Outbreak of adverse reactions associated with contaminated heparin. N Engl J Med 359:2674-2684, 2008

25. Combating counterfeit drugs. Lancet 371:1551, 2008